Phosphoric Acid Derivatives Category
Test Plan and Data Assessment

201-16174A

1. Category Chemicals.

Tris(2-ethylhexyl) phosphate (CAS# 78-42-2)
Bis(2-ethylhexyl) hydrogen phosphate (CAS# 298-07-7)
2-Ethylhexyl phosphate (CAS# 12645-31-7)*
Triisobutyl phosphate (CAS# 126-71-6)
Mono (2-ethylhexyl) phosphate (CAS# 1070-03-7)**
Dibutyl hydrogen phosphate (CAS# 107-66-4)**
Tributyl phosphate (CAS# 126-73-8)**
2-Ethylhexanol (CAS# 104-76-7)**
2-Ethylhexanoic acid (CAS# 149-57-5)**
Phosphoric Acid (CAS# 7664-38-2)**

* Mixture of CAS# 298-07-7 and CAS# 1070-03-7.
** Not sponsored as part of the EPA HPV Challenge Program; used only for data surrogate purposes.

2. Category Justification.

The Panel believes that there is adequate justification for including all of the chemicals in the Phosphoric Acid Derivatives Category for all end points. The Panel does not agree that the mono- and tri-esters should be treated as independent chemicals. Justification for the category is as follows:

2.1 The chemicals in this category have a similar chemical structure (Figure 1). They are alkyl esters of phosphoric acid. The four sponsored chemicals contain either 2-ethyl hexyl groups or isobutyl groups that are attached a phosphoric acid moiety forming mono-, di-, or tri-esters. The chemical described as 2-ethylhexyl phosphate (CAS# 12645-31-7) is a mixture of mono (2-ethylhexyl) phosphate (CAS# 1070-03-7) and bis (2-ethylhexyl) phosphate (CAS# 298-07-7). The chemicals described as bis(2-ethylhexyl) hydrogen phosphate (CAS# 298-07-7), tris (2-ethylhexyl) phosphate (CAS# 78-42-2) and triisobutyl phosphate (CAS# 126-71-6) are di- and tri-esters, respectively.

2.2 Dealkylation is expected based on the reaction chemistry (Figures 2 and 3). The reaction chemistry provides the foundation of support for the category and validates the read across between the tri-ester, di-ester, and mono-ester. The synthesis pathway of 2-ethylhexyl phosphate is similar to the pathway of triphenyl phosphate. Triphenyl phosphate is manufactured by the reaction of 3 moles of phenol and a mole of a pentavalent phosphorus species such as $POCl_3$, P_2O_5, etc. However, the reaction only proceeds to form the mono- and di-ester species. The content of the tri-ester species is <1%. The kinetics of the synthetic route favors the formation of the mono-ester, preceded by the di-ester, with the tri-ester species being the most difficult to obtain (See Figure 2).

Based on ester chemistry, the expected degradation/ hydrolysis pathway would be tri-ester to di-ester to mono-ester back to the starting materials. It is generally known that the more difficult an ester is to make, the more difficult it is to break. Therefore, it can be inferred that the hydrolysis step from the tri-ester to di-ester would require more energy than the di-ester to mono-ester hydrolysis, and so on.

While the BUA (1992) only grouped tri- and di-esters, the chemistry provides a strong basis that supports read across of the data from the tri- to di- to mono-esters. As described below, the preferred degradation/ hydrolysis pathway based on the reaction chemistry is tri-ester to di-ester to mono-ester and back to the starting materials.

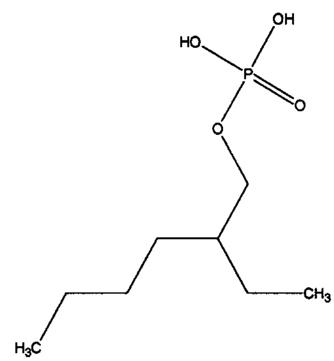
2.3 Phosphoric acid esters are metabolized via dealkylation. Metabolism studies conducted on the tributyl phosphate indicate that dealkylation to form the alkyl alcohol is the primary route of metabolism (WHO, 1991). The BUA (1992) reports that the phosphoric acid tri-esters are rapidly metabolized to di-esters with mono-diesters also being produced. Studies of tributyl phosphate show that 40-64% of the parent compound is metabolized to dibutyl dihydrogen phosphate and that 11- 21% is metabolized to the monobutyl species. Therefore, tris(2-ethylhexyl) phosphate is expected to be metabolized to bis(2-ethylhexyl) phosphate (CAS# 298-07-7) and mono(2-ethylhexyl) phosphate (CAS# 1070-03-7). Based on the evidence for dealkylation as the primary metabolic pathway, 2-ethylhexanol is the expected metabolite of tris(2-ethylhexyl) phosphate (CAS# 78-42-2) and 2-ethylhexyl phosphate (CAS# 12645-31-7). Triisobutyl phosphate is expected to be metabolized similarly as tributyl phosphate, with methoxypropanol as the alcohol metabolite.

2.4 2-Ethylhexyl phosphate (CAS# 12645-31-7) is a mixture of bis(2-ethylhexyl) phosphate (CAS# 298-07-7) and mono(2-ethylhexyl) phosphate (CAS# 1070-03-7). Based on metabolic information on phosphoric acid ester metabolism tris(2-ethylhexyl) phosphate is expected to undergo dealkylation to form 2-ethylhexyl phosphate (CAS#12645-31-7), a mixture of bis(2-ethylhexyl) phosphate (CAS# 298-07-7) and mono(2-ethylhexyl) phosphate (CAS# 1070-03-7).

2.5 Dealkylation of tri-, di-, and mono-(2-ethylhexyl) phosphate esters are expected to result in the formation of 2-ethylhexanol and phosphoric acid. The BUA (1997) review of bis(2-ethylhexyl) phosphate and tris(2-ethylhexyl) phosphate notes that 2-ethylhexanol is the presumptive metabolite. WHO (1991) notes that environmental biodegradation of tributyl phosphate involves a stepwise enzymatic hydrolysis to the orthophosphate and butanol.

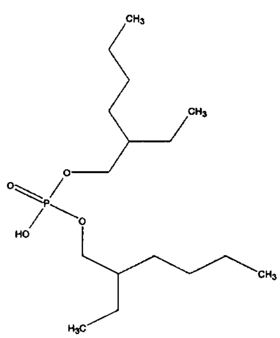
2.6 2-Ethyhexanol is known to be metabolized to 2-ethylhexanoic acid. The primary metabolite of 2-ethylhexanol is 2-ethylhexanoic acid. In metabolism studies using radiolabeled 2-ethylhexanol, Albro (1975) determined that 2-ethylhexanoic acid accounted for 61% of the acid fraction radioactivity or 46% of the total administered dose.

Figure 1. Chemical Structures

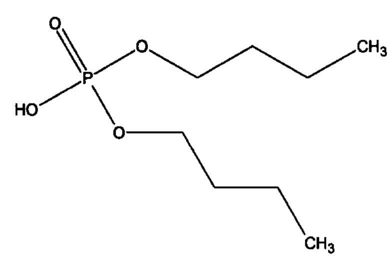


2-ethylhexyl phosphate
(Mono and Diester)
CAS # 12645-31-7

2-ethylhexyl Phosphate
(Monoester)
CAS# 1070-03-7

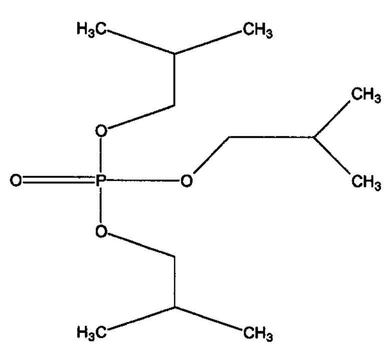


bis (2-ethylhexyl) phosphate
(Diester)
CAS # 298-07-7



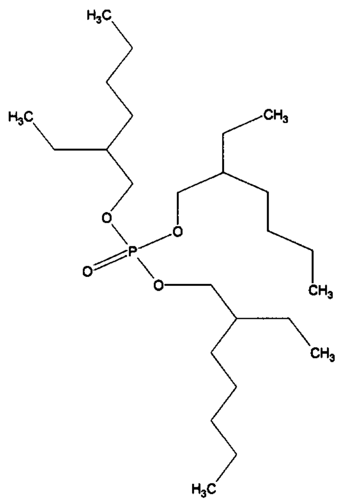
dibutyl hydrogen phosphate

CAS # 107-66-4

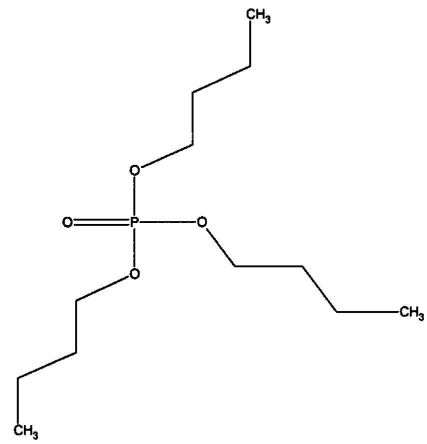


Triisobutyl phosphate
CAS# 126-71-6

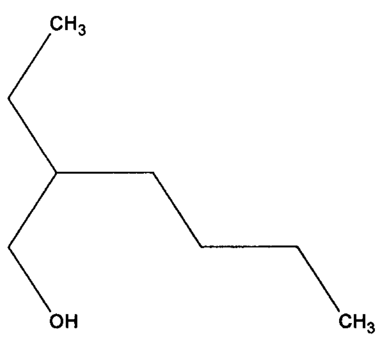
Figure 1. Chemical Structures(cont)



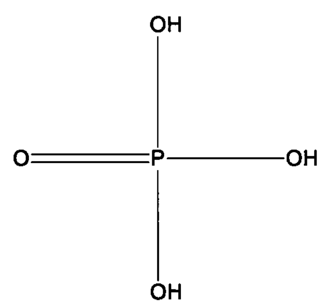
tris (2-ethylhexyl) phosphate
CAS # 78-42-2



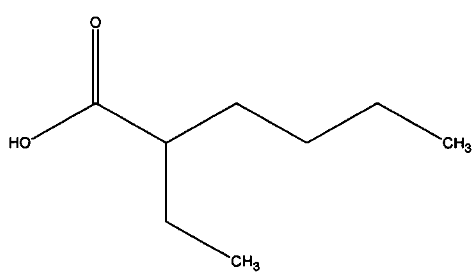
tributyl phosphate
CAS # 126-73-8



2-ethylhexanol
CAS# 104-76-7

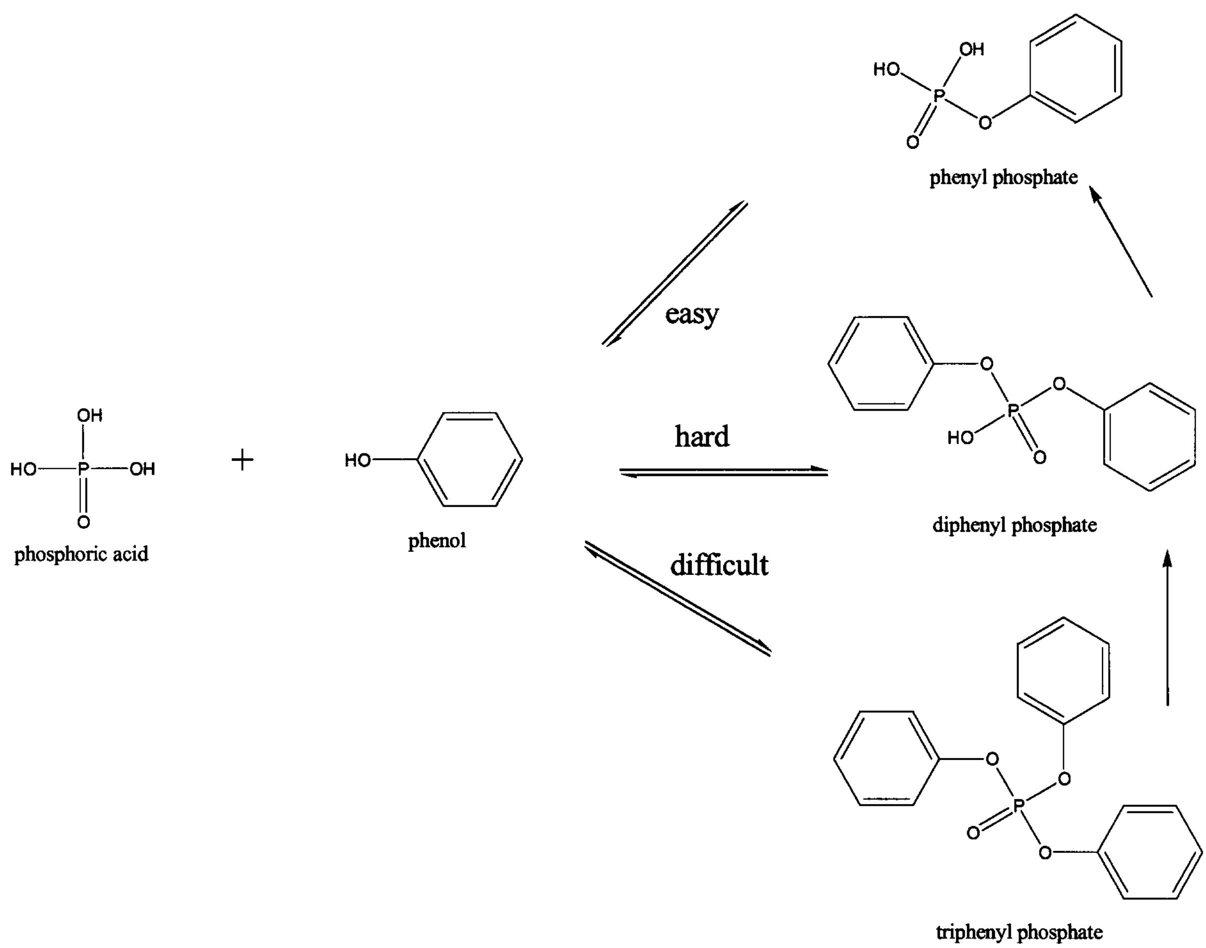


phosphoric acid
CAS# 7664-38-2



2-ethylhexanoic acid
CAS# 104-76-7

Figure 2. Reaction Chemistry and Hydrolysis Pathway



3.0 Physicochemical Properties and Environmental Fate.

The physicochemical properties and environmental fate of the chemicals in this category are similar with few exceptions as shown in Table 1. They have a low melting point, a high boiling point or decomposition temperature, and low vapor pressure. The tri-esters are slightly soluble and the others are moderately soluble to soluble in water. The results of the hydrolysis studies with 2-ethylhexyl phosphate (CAS# 12645-31-7), and triisobutyl phosphate (CAS# 126-71-6), and tributyl phosphate (CAS#126-73-8) indicate that the mono-, di-, and tri-esters all are hydrolytically stable. Fugacity Level III calculations indicate that if they are released into the environment, they will exist predominantly in the soil and/or soil or the aquatic environment depending on the environmental compartment that they first contact. 2-Ethylhexyl phosphate, bis(2-ethylhexyl) phosphate, and triisobutyl phosphate all exhibit appreciable biodegradation in 28 days or sooner indicating that they are moderately degradable and will not persist in the environment. Tris(2-ethylhexyl) phosphate, which has limited solubility in water, exhibited 0% biodegradation after 28 days in the OECD 301D closed bottle test.

4.0 Ecological Effects.

Studies of the ecotoxicity of the chemicals in this category indicate that none of the members are highly toxic to aquatic species. The fish 96-hour LC_{50} values ranged from >500 mg/l in *O. latipes* and >100 mg/l in *O. mykiss* for 2-ethylhexyl phosphate to 23 mg/l in *O. mykiss* for triisobutyl phosphate. The invertebrate 48-hour EC_{50} values with Daphnia ranged from 110 mg/l for 2-ethylhexyl phosphate to 11 mg/l for triisobutyl phosphate. The algal 96-hour EC_{50} values ranged from 4.4 mg/l with tributyl phosphate in *S. capricornutum* and to 161 mg/l with 2-ethylhexylphosphate in *S. capricornutum.*

5.0 Health Effects.

The chemicals in this category exhibit a low to moderate order of acute toxicity. The rat oral LD_{50} values ranged from 500-1000 mg/kg with 2-ethylhexyl phosphate to >36,800 mg/kg for tris(2-ethylhexyl) phosphate. The dermal LD_{50} values ranged from 1200 to > 2000 mg/kg (rat) with bis(2-ethylhexyl) hydrogen phosphate to ~ 20,000 mg/kg (rabbit) with tris(2-ethylhexyl) phosphate. The inhalation LC_{50} values ranged from > 0.447 mg/l (4hr. rat) with tris(2-ethylhexyl) phosphate to > 5.14 mg/l (4hr. rat) with triisobutyl phosphate. Oral repeat dose NOAEL's in rats for dibutyl hydrogen phosphate, tributyl phosphate, ethylhexanol, 2-ethylhexanoic acid, bis(2-ethylhexyl) hydrogen phosphate, tris(2-ethylhexyl) phosphate, and triisobutyl phosphate were 30 mg/kg/day (44 days), 75 mg/kg/day (90 days), 125 mg/kg/day (90 days), 100 mg/kg/day (90 days), 250 mg/kg/day (5 days), and 1000 mg/kg/day (90 days), and 68.4-84.3 mg/kg (90 days), respectively. Oral repeat dose NOAEL's in rats for dibutyl hydrogen phosphate, tributyl phosphate, ethylhexanol, 2-ethylhexanoic acid, tris(2-ethylhexyl) phosphate, and triisobutyl phosphate were 30 mg/kg/day (44 days), 75 mg/kg/day (90 days), 125 mg/kg/day (90 days), 100 mg/kg/day (90 days), and 1000 mg/kg/day (90 days), and 68.4-84.3 mg/kg (90 days), respectively.

The weight of the evidence indicates that the members of this category are not genotoxic. Tris(2-ethylhexyl) phosphate, bis(2-ethylhexyl) hydrogen phosphate, 2-ethylhexyl phosphate, dibutyl hydrogen phosphate, tributyl phosphate, triisobutyl phosphate, 2-ethylhexanol, 2-ethylhexanoic acid, and phosphoric acid were negative in the Ames assay. Tris(2-ethylhexyl) phosphate, bis(2-ethylhexyl) phosphate, 2-ethylhexyl phosphate, and 2-ethylhexanol also were negative in the mouse lymphoma assay. Furthermore, tris(2-ethylhexyl) phosphate, dibutyl hydrogen phosphate, tributyl phosphate, and 2-ethylhexanol were negative in the chromosomal aberration assays (*in vitro* and/or *in vivo*). Tris(2-ethylhexyl) phosphate was negative in a sister chromatid exchange assay while 2-ethylhexanoic acid was positive. Triisobutyl phosphate was negative in the *in vivo* mouse micronucleus assay.

Reproductive toxicity was evaluated with a number of the members of this category. No effects on reproductive organs were observed in repeat dose studies with tris(2-ethylhexyl) phosphate, dibutyl hydrogen phosphate, tributyl phosphate, 2-ethylhexanol, or 2-ethylhexanoic acid. A two generation reproduction study with tributyl phosphate did not find any reproductive effects in rats at the highest dose tested (225 mg/kg/day). No significant effects on reproduction were seen in rats with an oral OECD 422 combined repeat dose toxicity and reproductive/developmental toxicity screen with dibutyl hydrogen phosphate (NOAEL = 1000 mg/kg). Reproductive effects were reported in rats at 300 mg/kg/day and 600 mg/kg/day in a one generation study with 2-ethylhexanoic acid.

A number of the members of this category was evaluated for developmental toxicity. The developmental toxicity of tributyl phosphate was evaluated in both rats and rabbits. Tributyl phosphate and triisobutyl phosphate were determined not to be teratogenic. 2-Ethylhexanol was found to cause developmental toxicity only at doses that were maternally toxic. Drinking water and gavage developmental toxicity studies have also been conducted with 2-ethylhexanoic acid in rats and rabbits. Pannanen et al. (1992) reported developmental effects in rats at concentrations as low as 100 mg/kg administered in drinking water. Hendrickx et al. (1993) in their developmental studies with rats and rabbits concluded that 2-ethylhexanoic acid did not produce developmental effects in rats or rabbits under the conditions of these tests. The authors noted that the rat NOAEL was 100 mg/kg/day based on slight fetotoxicity at 250 mg/kg/day and that the rabbit NOAEL was 250 mg/kg/day (highest dose). The maternal NOAEL's for rats and rabbits were 250 mg/kg/day and 25 mg/kg/day, respectively.

6.0 Production Volume, Physical Form of Marketed Product and Use Pattern

The alkyl phosphates supported by the Phosphoric Acid Derivatives Panel are produced at 5 sites. Their physical form when sold is a liquid.

Production volume ranges from the 1986-2002 IUR are presented in Table 1.

Table 1 IUR Production Volume Ranges:

CAS No.	1986 Range	1990 Range	1994 Range	1998 Range	2002 Range	Chemical Name
12645317	10K-500K	>1M-10M	>1M-10M	>1M-10M	>1M-10M	Phosphoric acid, 2-ethylhexyl ester
298077	>1M-10M	>1M-10M	>1M-10M	>1M-10M	>1M-10M	Phosphoric acid, bis (2-ethylhexy) ester
78422	>1M-10M	>1M-10M	>500K-1M	>1M-10M	>500K-1M	Phosphoric acid, tris (2-ethylhexy) ester
126716	10K-500K	10K-500K	10K-500K	>500K-1M	>1M-10M	Phosphoric acid, tris (isobutyl) ester

Alkyl phosphates are used in industrial applications as PVC plasticizers (affording some flame retardancy), as defoamers in pulp and paper production and for oil field drilling needs. They can be used as antifoam agents in floor polishes, waxes and paper coating. Some alkyl phosphates are used lubricant additives and adhesive promoters, and for corrosion protection in coatings. They can be used in closed systems as chemical intermediates.

2-Ethylhexyl phosphate (12645-31-7) is used as an anti-wear component in industrial and automotive gear oil additive (GOA) packages at concentrations of approximately 4-30% of the GOA package and up to 15% of the final finished gear oil depending upon the end-use application of the lubricant.

Bis (2-ethylhexyl) phosphate (298-07-7) is used as a component in industrial and automotive gear oil additive packages at concentrations of approximately 4-30% of the GOA package and up to 15% of the final finished gear oil. It can also be used as an industrial metal extraction agent and in the production of nylon.

Tris (2-ethylhexl) phosphate (78-42-2) is used in catalysts for polypropylene at concentrations of approximately 1%.

Tri(isobutyl)phosphate (126-71-6) is used as a solvent as an antifoam agent, in hydraulic fluids, extraction agents and for the production of plastics.

Fugacity Level III calculations indicate that if they are released into the environment, they will exist predominantly in the soil and/or soil or the aquatic environment depending on the environmental compartment that they first contact. The Log_{10} P_{ow} indicates that they will not bioconcentrate. They exhibit appreciable biodegradation in 28 days or sooner indicating that they are moderately degradable if soluble and will not persist in the environment (Table 2).

There is limited opportunity for environmental release during manufacture because closed systems are employed and the chemicals are stored and transported in closed tanks, tank cars, tank trucks or in small-amount drums. Environmental release during transport is possible in the event of a spill. The members of the Panel are not aware of any significant spills or releases to the environment.

There are no reported industrial exposure limits.

7.0 Robust Summaries.

The Panel has added new information and critical data. This information can be found in the individual dossiers (IUCLIDs)

8.0 Conclusion

Again, the Panel has given careful consideration to the animal welfare principles contained in the EPA's October 14, 1999, letter to HPV Challenge Program participants. As directed, the Panel has sought to maximize the use of existing data for scientifically appropriate related chemicals and structure-activity-relationships. Additionally, the Panel has conducted a thoughtful, qualitative analysis rather than use a rote checklist approach in analyzing the adequacy of existing data. The Panel also has added additional information from the testing that it has conducted to fulfill all the Screening Information Data Set (SIDS) endpoints of the HPV program. The Panel believes these data are adequate to satisfy the requirements of the HPV program (see Table 1).

9.0 References

Albro, P.W. (1975). The metabolism of 2-ethylhexanol in rats. Xenobiotica 5(10):625-636.

BUA Report (1992). Existing Chemicals of environmental Relevance III: Priority Setting and Classified Existing Chemicals of the Third Priority List, edited by the GDCh-Advisory

BUA Report (1997). Di(2-ethylhexyl phosphate, Tri(2-ethylhexyl) phophate, Beratergremium fur Umweltrelevante Altstoffe, 172, pp. 1-125.

Advisory Committee on Existing Chemicals of Environmental Relevance, Beratergremium fur Umweltrelevante Altstoffe, pp. 37.

Hendrickx et al. (1993). Assessment of the developmental toxicity of 2-ethylhexanoic acid in rats and rabbits. Fund. Appl. Toxicol. 20:199-209.

Pennanen et al. (1992). The developmental toxicity of 2-ethylhexanoic acid in Wistar rats. Fund. Appl. Toxicol. 19:505-511.

WHO Working Group (1991). Tri-n-butyl phosphate, Environmental Health Criteria, 112, pp. 1-80.

Table 1. Matrix of Available and Adequate Data on the Phosphoric Acid Derivatives Category Physico-chemical Properties

Endpoint	2-Ethyl hexyl phosphate 12645-31-7	Mono (2-ethyl hexyl) phosphate 1070-03-7	2-Ethylhexanol 104-76-7	2-Ethylhexanoic Acid 149-57-5	Phosphoric acid 7664-38-2	Dibutyl hydrogen phosphate 107-66-4	Tributyl phosphate 126-73-8	Triisobutyl phosphate 126-71-6	Bis (2-ethyl hexyl) phosphate 298-07-7	Tris (2-ethyl hexyl) phosphate 78-42-2
Molecular Weight:	210.21 322.43	210.21	130.22	144.22	98	210.21	266.32	266.32	322.43	434.65
Melting Point	< 253°K (< -20°C)	No Data	-76°C	<-60°C	42.4°C	-13°C	<-70°C	<-60°C	-50°C	<-70°C
Boiling Point	(Decomp.) 354°C@1013 hPa (EPI)	(Decomp.) 354°C@1013 hPa (EPI)	184.3°C @1013 hPa	228°C @1013 hPa	133-213 °C@1013 hPa	>200°C@20 hPa 319°C@1013 hPa (EPI)	130°C@5 hPa 327°C@1013 hPa (EPI)	115°C@ 30 hPa 272°C @1013 hPa 302°C (EPI)	240°C@ 1013 hPa (Decomp.) 400°C@ 1013 hPa (EPI)	>210°C@5 hPa (Decomp.) 446°C@1013 hPa (EPI)
Relative Density	1.05g/cm3 @ 20°C	1.05g/cm3 @ 20°C	0.834g/cm3 @ 20°C	0.906g/cm3 @ 20°C	1.58-1.7@20°C	1.05g/cm3 @ 20°C	0.97g/cm3 @20°C	0.965g/cm^3 @ 20° C	0.96g/cm^3 @ 20° C	0.92g/cm3 @20°C
Vapor Pressure	7.12 x10(-7) hPa @25°C (EPI)	5.34 x10(-7) hPa @25°C (EPI)	0.4 hPa @20°C	0.04 hPa @20°C	0.038 hPa@20°C	2.42 x10(-5) hPa @25°C (EPI) <0.1 hPa @20°C	3.47 x10(-6) hPa @25°C (EPI)	1.00 @ 91.74 °C 1.28 x10(-2) hPa @25°C (EPI)	2.4 x10(-7) hPa @25°C (EPI)	2.05 x10(-7) hPa @25°C (EPI)
Partition Coefficient	2.65 (EPI)	2.65 (EPI)	3.1	2.64	-0.77	0.6-1.4 2.2 (EPI)	2.5 3.8 (EPI)	3.72@25°C 3.6 (EPI)	2.67	4.2 9.49 (EPI)
Water Solubility	2.19x10^3 mg/l @25°C 182 mg/l @25°C	2.19x10^3 mg/l @25°C	1.1 g/l @25°C	1.4 g/l @20°C	1.5 g/l@25°C	18 g/l@20°C 430 mg/l @ 25°C (EPI)	0.4 g/l@20°C 7.35 mg/l @ 25°C (EPI)	0.265 g/l 16.22 mg/l@ 25°C (EPI)	210 mg/l @ 20°C	2 mg/l 0.01 mg/l @ 25°C (EPI)

[shaded box] = Non-sponsored chemicals used for data purposes only

EPI = EPIWin Modeling Program. Meylan W. and Howard P. (1999) Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510; EPI Suite™ v3.10 Copyright 2000.

Table 2. Matrix of Available and Adequate Data on the Phosphoric Acid Derivatives Category
Environmental Fate

Endpoint	2-Ethyl hexyl phosphate 12645-31-7	Mono (2-ethyl hexyl) phosphate 1070-03-7	2-Ethylhexanol 104-76-7	2-Ethylhexanoic Acid 149-57-5	Phosphoric acid 7664-38-2	Dibutyl hydrogen phosphate 107-66-4	Tributyl phosphate 126-73-8	Triisobutyl phosphate 126-71-6	Bis (2-ethyl hexyl) phosphate 298-07-7	Tris (2-ethyl hexyl) phosphate 78-42-2
Photo-degradation	$T_{1/2}$ = 3.9 hr (AOP)	$T_{1/2}$ = 3.9 hr (AOP)	$T_{1/2}$ = 9.9 hr (AOP)	$T_{1/2}$ = 16 hr (AOP)	$T_{1/2}$ = 25.5 days (AOP)	$T_{1/2}$ = 2.4 hr (AOP)	85% after 1 hr. (UV) $T_{1/2}$ = 1.6 hr (AOP)	$T_{1/2}$ = 4.3 hr (AOP)	$T_{1/2}$ = 3.9 hr (AOP)	80% after 1 hr (UV) $T_{1/2}$ = 1.3 hr (AOP)
Hydrolysis	$T_{1/2}$ = > 1 yr	No Data	No Data	No Data	No Data	No Data	No hydrolysis after 30 days at any pH	$T_{1/2}$ = ca. 170d@ 0°C, pH = 4 $T_{1/2}$ = ca. 303d@50°C ,pH = 7	No Data	No Data
Biodegradation	52% after 28 days	No Data	95-100 % after 5 days	39 % after 28 days	No Data	12 % after 28 days	77-92 % after 28 days	97% after 14 days	75 % after 28 days	0 % after 28 days
Fugacity Level III (distribution)	EPIWIN	EPIWIN	EPIWIN (Calculated)	EPIWIN	EPIWIN	EPIWIN	EPIWIN	EPIWIN	EPIWIN	EPIWIN
Air	< 0.1 %	< 0.1 %	4.24 % (16 %)	5.29 %	0.000824 %	0.183 %	0.0737 % (11)	0.518%	0.302 %	0.31 %
Water	29 %	29 %	41.2 % (53 %)	41.6 %	45.3 %	34.4 %	41 % (58)	38.8%	24.5 %	10.9 %
Soil	70.8 %	70.8 %	54.3 % (25 %)	53 %	54.7 %	65.3 %	56.7 % (16)	59.5%	75 %	31.2 %
Sediment	0.188 %	0.188 %	0.216 % (5.4 %)	0.197 %	0.0755 %	0.112 %	1.52 % (15)	1.14%	0.226 %	57.6 %

= Non-sponsored chemicals used for data purposes only

EPI = EPIWin Modeling Program. Meylan W. and Howard P. (1999) Syracuse Research Corporation.
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Table 3. Matrix of Available and Adequate Data on the Phosphoric Acid Derivatives Category

Ecotoxicity

Endpoint	2-Ethyl hexyl phosphate 12645-31-7	Mono (2-ethyl hexyl) phosphate 1070-03-7	2-Ethylhexanol 104-76-7	2-Ethylhexanoic Acid 149-57-5	Phosphoric acid 7664-38-2	Dibutyl hydrogen phosphate 107-66-4	Tributyl phosphate 126-73-8	Triisobutyl phosphate 126-71-6	Bis (2-ethyl hexyl) phosphate 298-07-7	Tris (2-ethyl hexyl) phosphate 78-42-2
Acute Fish Toxicity (96 hr LC50)	>100 mg/l *O. mykiss*	No Data	29.7 mg/l *P. promelas* >7.5 mg/l *O. mykiss* 32-37 mg/l *S. gairdner*	180 mg/l *S. gairdneri* (nominal conc.))	3.0-3.5 pH *L. macrochris* 29.7 mg/l *P. promelas*	>100 mg/l >10,000 mg/l *B. rerio*	13 mg/l *O. mykiss* 10-14 mg/l *B. rerio*	23 mg/l *O. mykiss*	30 mg/l *S. gairdneri*	>500 mg/l *O. latipes* >100 mg/l *B. rerio*
Acute Invertebrate Toxicity (48 hr EC50)	110 mg/l *D. magna*	No Data	39 mg/l *D. magna*	85.4 mg/l *D. magna*	4.6 mg/l *D. magna* *(12 hr)*	90.9 mg/l *D. magna*	*2.6-9.0 mg/l* *D. magna*	11 mg/l *D. magna*	60.7 mg/l *D. magna*	No Data
Algal Toxicity (96 hr EC50)	161 mg/l *S. capricor-nutum* (72 hr EC50)	No Data	11.5 mg/l *S. subspicatus*	41 mg/l *S. subspicatus*	No Data	No Data	4.4 mg/l *S. capricor-nutum*	30 mg/l *S. subspicatus*	> 100 mg/l *C. emersonii*	No Data

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Table 4. Matrix of Available and Adequate Data on the Phosphoric Acid Derivatives Category Acute Mammalian Toxicity

Endpoint	2-Ethyl hexyl phosphate 12645-31-7	Mono (2-ethyl hexyl) phosphate 1070-03-7	2-Ethylhexanol 104-76-7	2-Ethylhexanoic Acid 149-57-5	Phosphoric acid 7664-38-2	Dibutyl hydrogen phosphate 107-66-4	Tributyl phosphate 126-73-8	Triisobutyl phosphate 126-71-6	Bis (2-ethyl hexyl) phosphate 298-07-7	Tris (2-ethyl hexyl) phosphate 78-42-2
Acute Oral LD50	500-1000 mg/kg (rat)	2710 mg/kg (rat)	1516-7000 mg/kg (rat) 2500-4460 mg/kg (mouse)	2000-3640 mg/kg (rat)	1530 mg/kg (rat)	2000 mg/kg (rat)	1390-11,265 mg/kg (rat)	>5,000 mg/kg (rat)	1400-4742 mg/kg (rat)	>36,800 mg/kg (rat) >46,000 mg/kg (rabbit)
Acute Dermal LD50	No Data	>4,640 mg/kg (rabbit)	3000 mg/kg (rabbit)	>2000 mg/kg (rabbit)	2740 mg/kg (rabbit)	No Data	> 3,100- >10,000 mg/kg (rabbit)	>5,000 mg/kg (rabbit)	1200 - >2000 mg/kg (rat)	~20,000 mg/kg (rabbit)
Acute Inhalation LC50	No Data	No Data	0.89 mg/l LC_0 (4hr., rat) 227 ppm LC_0 (6 hr., rat)	2.36 mg/l LC_0 (6hr., rat) >2.39 mg/l LC_0 (6 hr., g. pig)	No Data	No Data	>4.242 mg/l (4hr., rat) >42 mg/l (6hr., rat)	>5.14 mg/l (4hr, rat)	No Data	> 0.447 mg/l (4 hrs., rat)

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Table 5. Matrix of Available and Adequate Data on the Phosphoric Acid Derivatives Category Genotoxicity

Endpoint	2-Ethyl hexyl phosphate 12645-31-7	Mono (2-ethyl hexyl) phosphate 1070-03-7	2-Ethylhexanol 104-76-7	2-Ethylhexanoic Acid 149-57-5	Phosphoric acid 7664-38-2	Dibutyl hydrogen phosphate 107-66-4	Tributyl phosphate 126-73-8	Triisobutyl phosphate 126-71-6	Bis (2-ethyl hexyl) phosphate 298-07-7	Tris (2-ethyl hexyl) phosphate 78-42-2
Mutagenicity/ Gene Mutation	Ames Negative (2 studies) Mouse Lymphoma Negative	No Data	Ames Negative Mouse Lymphoma Negative	Ames Negative	Ames Negative	Ames Negative	Ames Negative (5 of 6 studies) *E. coli* Negative CHO Negative	Ames Negative	Ames Negative Mouse Lymphoma Negative	Ames Negative Mouse Lymphoma Negative
Mutagenicity/ Chromosome Aberration	No Data	No Data	Chrom. Aber. (rat) Negative	Sister Chromatid Exchange Positive	No Data	Chrom. Aber. (CHL) Negative Micronucleus test (mouse) Negative	Chrom. Aber. (CHO) Negative *In vivo* Cytogen-etic (rat) Negative Drosophila SLRL Negative	*In vivo* Cytogenetic (mouse) Negative	No Data	Chrom. Aber. (CHO) Negative Sister Chromatid Exchange Negative

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Table 6. Matrix of Available and Adequate Data on the Phosphoric Acid Derivatives Category Mammalian Repeat Dose, Reproductive and Developmental Toxicity

Endpoint	2-Ethyl hexyl phosphate 12645-31-7	Mono (2-ethyl hexyl) phosphate 1070-03-7	2-Ethylhexanol 104-76-7	2-Ethylhexanoic Acid 149-57-5	Phosphoric acid 7664-38-2	Dibutyl hydrogen phosphate 107-66-4	Tributyl phosphate 126-73-8	Triisobutyl phosphate 126-71-6	Bis (2-ethyl hexyl) phosphate 298-07-7	Tris (2-ethyl hexyl) phosphate 78-42-2
Repeat Dose (NOAEL)	No Data	No Data	125 mg/kg (3 m. gav. rat) 125-250 mg/kg (3 m. gav. mouse) 120 ppm (90-D inh. rat)	100 mg/kg (90 day. oral feed, rat) 150 mg/kg (90 day. oral feed, mouse)	No Data	30 mg/kg (oral, rat, 44 days)	75 mg/kg (female) 15 mg/kg (male) (oral, rat, 13 wk)	68.4-84.3 mg/kg (oral, rat, 13 wk)	250 mg/kg (5-day oral feed, rat	1000 mg/kg (oral, rat, 13wk) 430 mg/kg (oral, rat, 30D) 1.6 mg/m^3 (Inh. gp, 90D)
Reproductive Toxicity (NOAEL)	No Data	No Data	No effect on reproductive organs in oncogenicity studies	300 mg/kg parental 100 mg/kg offspring	No Data	1000 mg/kg (oral, rat)	225 mg/kg (oral, rat)	No Data	No Data	No Data
Developmental Toxicity (NOAEL)	No Data	No Data	650 mg/kg (gavage, rat) >2520 mg/kg (dermal, rat)	<100 mg/kg (drinking water, rat) 100 mg/kg (gavage, rat) 250 mg/kg (gavage, rabbit)	No Data	No Data	>250 mg/kg (oral, rat) 400 mg/kg (oral, Rabbit)	1000 mg/kg (oral, rat)	No Data	No Data

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Table7. Summary of Data and Test Plan for the Phosphoric Acid Derivatives Category

Endpoint	2-Ethyl hexyl phosphate 12645-31-7	Mono (2-ethyl hexyl) phosphate 1070-03-7	2-Ethylhexanol 104-76-7	2-Ethylhexanoic Acid 149-57-5	Phosphoric acid 7664-38-2	Dibutyl hydrogen phosphate 107-66-4	Tributyl phosphate 126-73-8	Triisobutyl phosphate 126-71-6	Bis (2-ethyl hexyl) phosphate 298-07-7	Tris (2-ethyl hexyl) phosphate 78-42-2
Physical-Chemical Properties										
Melting Point	A	A	R	A	A	A	A	A	A	A
Boiling Point	C	C	C	A	A	A	A	A	A	A
Partition Coef.	C	C	C	A	A	A	A	A	A	A
Water Solubility	A	A	A	A	A	A	A	A	A	A
Environmental Fate										
Photodegradation	C	C	C	C	C	C	C	C	C	A
Hydrolysis	A	A	R	NR	NR	NR	NR	A	R	R
Biodegradability	A	A	R	A	A	NR	A	A	A	A
Fugacity	C	C	C	C	C	C	C	C	A	C
Ecotoxicology										
Fish Toxicity	A	A	R	A		A	A	A	A	A
Invertebrate Tox.	A	A	R	A	A	A	A	A	A	R
Algal Toxicity	A	A	R	A	A	NR	NR	A	A	R
Mammalian Toxicology										
Acute Toxicity	A	A	A	A	A	A	A	A	A	A
Gene mutation	A	A	R	A	A	A	A	A	A	A
Chromosome aberration	R	R	R	A	A	NR	A	A	R	A
Repeated Dose	R	R	R	A	A	NR	A	A	R	A
Reproductive Tox.	R	R	R	A	A	NR	A	R	R	R
Developmental Tox.	R	R	R	A	A	NR	NR	A	R	R

Key for symbols in table:
A = Adequate data available
R = Endpoint requirement fulfilled using category approach, SAR
C = Endpoint requirement fulfilled based on calculated data
T = Testing Proposed
NR = No testing required; chemical not sponsored
▒ = Non-sponsored chemicals used for data purposes only.